UNIVERSITY OF PAVIA
DEPARTMENT OF HEALTH SCIENCES – PSYCHIATRY SECTION
AUTISM UNIT

Autismo e problemi del comportamento: interventi riabilitativi e intervento farmacologico

Marianna Boso, Stefania Ucelli, Francesco Barale

Autismo in età adulta: bisogni, interventi e servizi.
Cesena, 27-28 Gennaio 2011

AUTISM

- a biologically based disorder
- diagnosed on the basis of difficulties in socialisation and communication
- people with autism also show repetitive behaviours and a desire for sameness
- narrow interests are commonly described → often talent in different fields, such as music

Non solo deficit…

- Isolotti di capacità → savant → prodigi (Treffert, 2009; Pring, 2005; Heaton, 2004)
- Sia in HF che in LF (Treffert, 2009)
- Musica, arte, calcolo/matematica, memoria
- Weak central coherence: vedono le parti piuttosto che l'insieme → miglior accesso ai dettagli e capacità di manipolarli → creatività (Happé, 1999)
- Tendenza attuale a ricercare elementi di autisticità in geni del passato (Fitzgerald, 2002)

Autism: cognitive deficit or cognitive style?

Francesca Happé

Autism is a developmental disorder characterized by impaired social and communicative development, and restricted interests and activities. This article will argue that we can discover more about developmental disorders such as autism through demonstrations of task success than through examples of task failure. Even in exploring and explaining what people with autism find difficult, such as social interaction, demonstration of competence on contrasting tasks has been crucial to defining the nature of the specific deficit. Deficit accounts of autism cannot explain, however, the assets seen in this disorder; for example, savant skills in maths, music and drawing, and islets of ability in visuospatial tests and rote memory. An alternative account, reviewed here, suggests that autism is characterized by a cognitive style biased towards local rather than global information processing – termed 'weak central coherence'. Evidence that weak coherence might also characterize the relatives of people with autism, and form part of the extended phenotype of this largely genetic disorder, is discussed. This review concludes by considering some outstanding questions concerning the specific cognitive mechanism for coherence and the neural basis of individual differences in this aspect of information processing.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B

Phil. Trans. R. Soc. B (2009) **364**, 1385–1391
doi:10.1098/rstb.2008.0333

Enhanced perception in savant syndrome: patterns, structure and creativity

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According to the enhanced perceptual functioning (EPF) model, autistic perception is characterized by: enhanced low-level operations; locally oriented processing as a default setting; greater activation of perceptual areas during a range of visuospatial, language, working memory or reasoning tasks; autonomy towards higher processes; and superior involvement in intelligence. EPF has been useful in accounting for autistic relative peaks of ability in the visual and auditory modalities. However, the role played by atypical perceptual mechanisms in the emergence and character of savant abilities remains underdeveloped. We now propose that enhanced detection of patterns, including similarity within and among patterns, is one of the mechanisms responsible for operations on human codes, a type of material with which savants show particular facility. This mechanism would favour an orientation towards material possessing the highest level of internal structure, through the implicit detection of within- and between-code isomorphisms. A second mechanism, related to but exceeding the existing concept of redintegration, involves completion, or filling-in, of missing information in memorized or perceived units or structures. In the context of autistics' enhanced perception, the nature and extent of these two mechanisms, and their possible contribution to the creativity evident in savant performance, are explored.

Keywords: autism; savant syndrome; perception; creativity; pattern recognition; redintegration

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B

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Talent in autism: hyper-systemizing, hyper-attention to detail and sensory hypersensitivity

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We argue that *hyper-systemizing* predisposes individuals to show talent, and review evidence that hyper-systemizing is part of the cognitive style of people with autism spectrum conditions (ASC). We then clarify the hyper-systemizing theory, contrasting it to the weak central coherence (WCC) and executive dysfunction (ED) theories. The ED theory has difficulty explaining the existence of talent in ASC. While both hyper-systemizing and WCC theories postulate *excellent attention to detail*, by itself excellent attention to detail will not produce talent. By contrast, the hyper-systemizing theory argues that the excellent attention to detail is directed towards detecting 'if p, then q' rules (or [input–operation–output] reasoning). Such law-based pattern recognition systems can produce talent in systemizable domains. Finally, we argue that the excellent attention to detail in ASC is itself a consequence of *sensory hypersensitivity*. We review an experiment from our laboratory demonstrating sensory hypersensitivity detection thresholds in vision. We conclude that the origins of the association between autism and talent begin at the sensory level, include excellent attention to detail and end with hyper-systemizing.

Keywords: autism; Asperger syndrome; savant

Le basi neurali 1

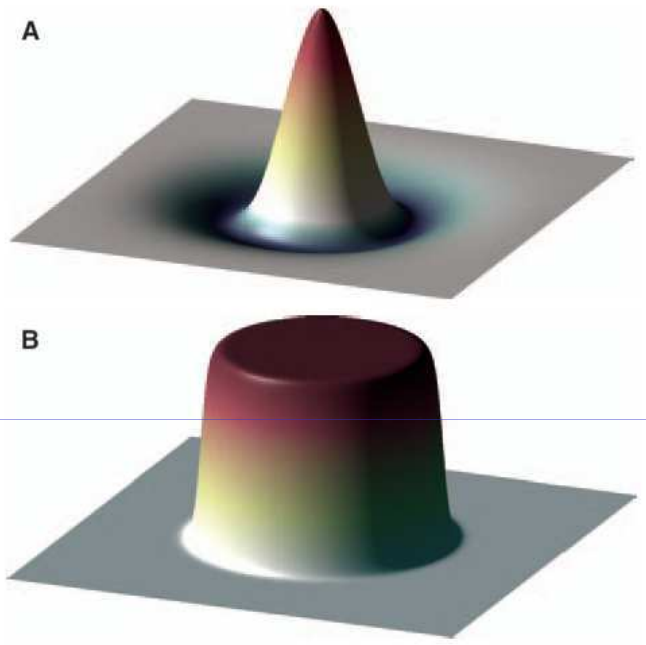

Fig. 1. Lateral inhibition can be visualized by plotting the net effect of a minicolumn's activation as a function of distance from that minicolumn, tangential to the cortical surface. When an idealized, healthy minicolumn is active (A), its short range output is a combination of excitatory (red) and inhibitory (blue) signals, which summed create a Mexican-hat profile of excitation/inhibition. Pathological minicolumns with an inhibition deficit mutually excite one another so that activation of any one tends to activate an entire module, resulting in a "stovepipe hat" profile (B).

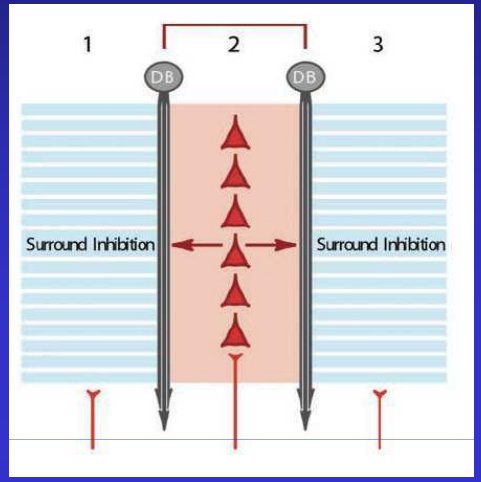

Table 1. GABAergic Abnormalities in Autism

- Alterations in platelet, plasma, and urine GABA levels
- Abnormalities in the gene coding for reelin[a] as well as in its tissue levels
- Abnormalities in the long arm of chromosome 15 (near a cluster of genes coding for GABA receptor subunits)
- A paradoxical effect of benzodiazepines on autistic individuals
- Reduced GABAergic receptor binding in the hippocampus
- Increased incidence of seizures

The table is a summary of evidence from Dhossche and others (2002).
[a] A glycoprotein involved in the regulation of GABAergic transmission.

Casanova, 2003, 2006, 2009

Deficit di connettività long-range

Molecular Psychiatry (2004) 9, 646–663

www.nature.com/mp

FEATURE REVIEW

Autism as a disorder of neural information processing: directions for research and targets for therapy[1]

MK Belmonte[1], EH Cook Jr[2], GM Anderson[3], JLR Rubenstein[4], WT Greenough[5], A Beckel-Mitchener[5], E Courchesne[6], LM Boulanger[7], SB Powell[8], PR Levitt[9], EK Perry[10], YH Jiang[11], TM DeLorey[12] and E Tierney[13]

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The broad variation in phenotypes and severities within autism spectrum disorders suggests the involvement of multiple predisposing factors, interacting in complex ways with normal developmental courses and gradients. Identification of these factors, and the common developmental path into which they feed, is hampered by the large degrees of convergence from causal factors to altered brain development, and divergence from abnormal brain development into altered cognition and behaviour. Genetic, neurochemical, neuroimaging, and behavioural findings on autism, as well as studies of normal development and of genetic syndromes that share symptoms with autism, offer hypotheses as to the nature of causal factors and their possible effects on the structure and dynamics of neural systems. Such alterations in neural properties may in turn perturb activity-dependent development, giving rise to a complex behavioural syndrome many steps removed from the root causes. Animal models based on genetic, neurochemical, neurophysiological, and behavioural manipulations offer the possibility of exploring these developmental processes in detail, as do human studies addressing endophenotypes beyond the diagnosis itself.
Molecular Psychiatry (2004) **9,** 646–663. doi:10.1038/sj.mp.4001499
Published online 23 March 2004

Keywords: autism; development; neurochemistry; genetics; animal models

E il cervelletto?

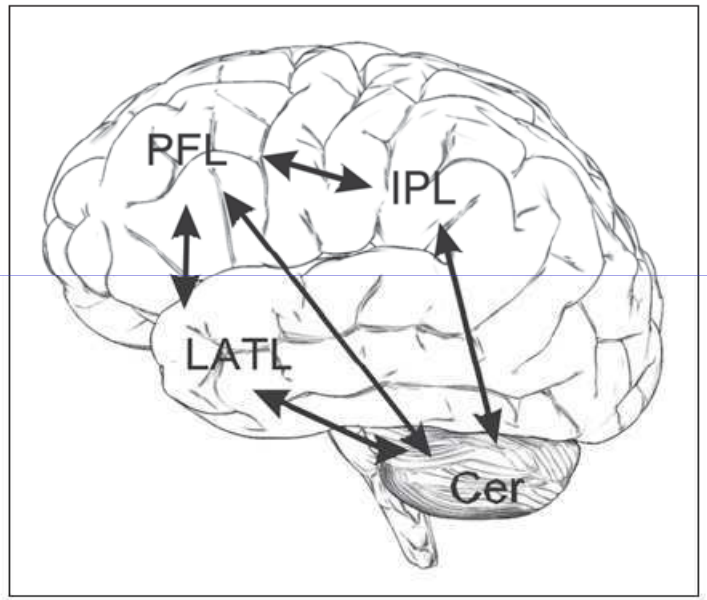


Figure 1 - Altered functional connectivity between the prefrontal lobe (PFL), inferior parietal lobe (IPL), left anterior temporal lobe (LATL) and cerebellum is considered to be at the basis of the autistic pathology.

Boso et al, Funct Neur, 2010

- Sono ipotizzabili alterazioni E/I anche qui (simili alla minicolonnopatia prefrontale)
- Meno cellule del Purkinje → disinibizione nuclei centrali → iperconnettività locale e ipoconnettività cerebello-talamo-PF e corticale in generale
- aumentato volume lobi prefrontali (e diminuito volume cerebellare)

Le basi neurali 2

Il concetto di minicolonnopatia (Casanova 2003, 2006, 2009) rende ragione degli aspetti nucleari patologici quali:

→ insistenza su dettagli e routine, ripetitività, sameness

→ difficoltà ad integrare gli impulsi: pattern comportamentali abnormi

→ isolamento sociale

Dovuti a scarsa connettività su vasta scala per l'eccessivo rumore di fondo (ipereccitazione)

Ma spiega anche il fenomeno del "talento autistico": insistenza sui dettagli → sviluppo di skills → perfezionamento delle stesse → talento

Gli interventi per le persone con autismo

L'integrazione delle persone autistiche presenta **difficoltà** connesse proprio al **loro essere autistiche: i problemi comunicativi e sociali sono il *core* del disturbo**.

Abilitazione e riabilitazione per le persone autistiche

- L'autismo è una condizione limite per le normali strategie della riabilitazione psicosociale.
- Qui sono i fondamenti stessi della socialità ad essere in questione.
- La generica immissione nella socialità di per sé non è affatto utile, spesso è dannosa.
- L'inclusione va governata tecnicamente e della socialità vanno in continuazione facilitate le condizioni.
- Ciò vale per i soggetti low functioning, ma anche per quelli high functioning (Howlin 2006, 2009).

Systematic Review of Early Intensive Behavioral Interventions for Children With Autism

Patricia Howlin and Iliana Magiati
Institute of Psychiatry, King's College (London, UK)

Tony Charman
University College, London, Institute of Child Health

Abstract

Recent reviews highlight limitations in the evidence base for early interventions for children with autism. We conducted a systematic review of controlled studies of early intensive behavioral interventions (EIBI) for young children with autism. Eleven studies met inclusion criteria (including two randomized controlled trials). At group level, EIBI resulted in improved outcomes (primarily measured by IQ) compared to comparison groups. At an individual level, however, there was considerable variability in outcome, with some evidence that initial IQ (but not age) was related to progress. This review provides evidence for the effectiveness of EIBI for some, but not all, preschool children with autism.

haviors. Although behavioral approaches are an important element of any comprehensive program (perhaps especially in the early years), other elements that focus more specifically on social development and communication will also be required for optimal effectiveness. This will also re-

There is good evidence now, from a number of randomized control trials (Aldred et al., 2004; Howlin et al., 2007; Kasari et al., 2006; Yoder & Stone, 2006), that other, nonintensive interventions, particularly those with a focus on communication and joint social interaction, can have a significant and positive impact on children's functioning. A switch of focus to examining the com-

- Ciò che è “naturalmente evidente” per le persone non autistiche (che non hanno problemi di coerenza centrale, di ToM, di EF, di decifrazione delle intenzioni...) deve essere “reso evidente” per le persone autistiche.
- E non è mai “evidente una volta per tutte”.

Occorre progettare non solo tecniche -dai risultati spesso instabili e non generalizzabili- ma interventi e contesti di vita pensati sulle caratteristiche dell'autismo:

→ i tipici problemi comunicativi, di ToM, di EF, di coerenza centrale

In tal modo anche quelle tecniche possono trovar migliore efficacia.

Interventi e contesti per l'autismo

- Per le persone autistiche ad elevato funzionamento, includibili in contesti comuni: lavoro di "mediazione culturale".

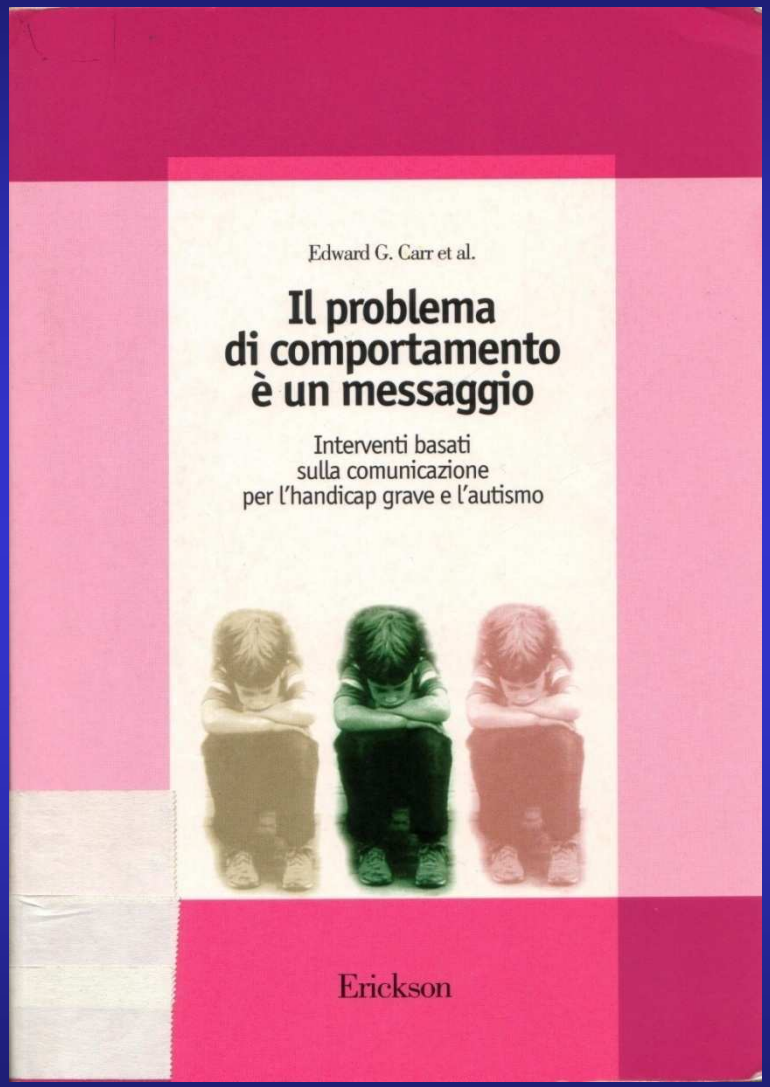
- Per le persone a basso funzionamento: "creazione" di contesti adatti, di vita e lavoro vero, non di "intrattenimento", che consentano una adultità autistica.

Comportamenti problema come messaggio

Il CP funziona spesso come
una forma primitiva di comunicazione
per soggetti che non possiedono ancora,
o non usano,
forme più sofisticate di comunicazione;

attraverso i CP possono influenzare gli altri
ottenendo una
serie di effetti desiderabili,
definiti rinforzatori.”

(Carr, 1994)



Carr, E.G. et al.(2005):

"Il problema di comportamento è un messaggio"

Alta prevalenza di CP

Correlata positivamente:

1. ad un basso QI

2. al sesso maschile
per i comportamenti eteroaggressivi

3. alla co-presenza di altre disabilità
motorie, visive;
ma soprattutto comunicative e di social-skills,
quelle più implicate nell'autismo

4. ai livelli ed alla precocità di istituzionalizzazione in contesti restrittivi
dato da non interpretare semplicisticamente nè in modo univoco

Alta prevalenza di CP

Correlata positivamente:

5. ad un eccesso oppure
ad un difetto di stimoli
contesti confusi o eccessivamente richiedenti
contesti poco significativi e demotivanti

6. all'età
tende a crescere progressivamente durante l'infanzia,
ha un picco tra i 15 e i 35 anni,
poi tende a declinare,
con differenze tra i singoli tipi di CP
e per sindromi

Cosa fare di fronte ad un CP

Innanzitutto, porsi delle domande

1. Che funzione o quali insieme di funzioni svolge quel determinato CP?
Comunicativa verso l'ambiente? Di autostimolazione?
Di modulazione del flusso sensoriale? Un misto di tutto ciò?

2. In quali occasioni è più frequente?
Ci sono delle ricorrenze evidenziabili?

3. Quali comportamenti positivi del repertorio del soggetto autistico potrebbero essere utilizzati in alternativa e/o essere incrementati?

Analisi funzionale

Analisi funzionale CP						
DATA	**ORA**	**Contesto generale**	**Contesto interpersonale**	**Comp. problema**	**Reazione operatore**	**Ipotesi** 1. Richiesta di attenzione 2. Fuga dal compito o situazione sgradita 3. Richiesta di oggetto gratificante

Le parole chiave dell'intervento riabilitativo

- Intervento ecologico
- Soggettività
- From shared action to shared mind → Problem solving condiviso
- Imitazione

- Intervento ecologico
- Soggettività
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Il principio "ecologico"

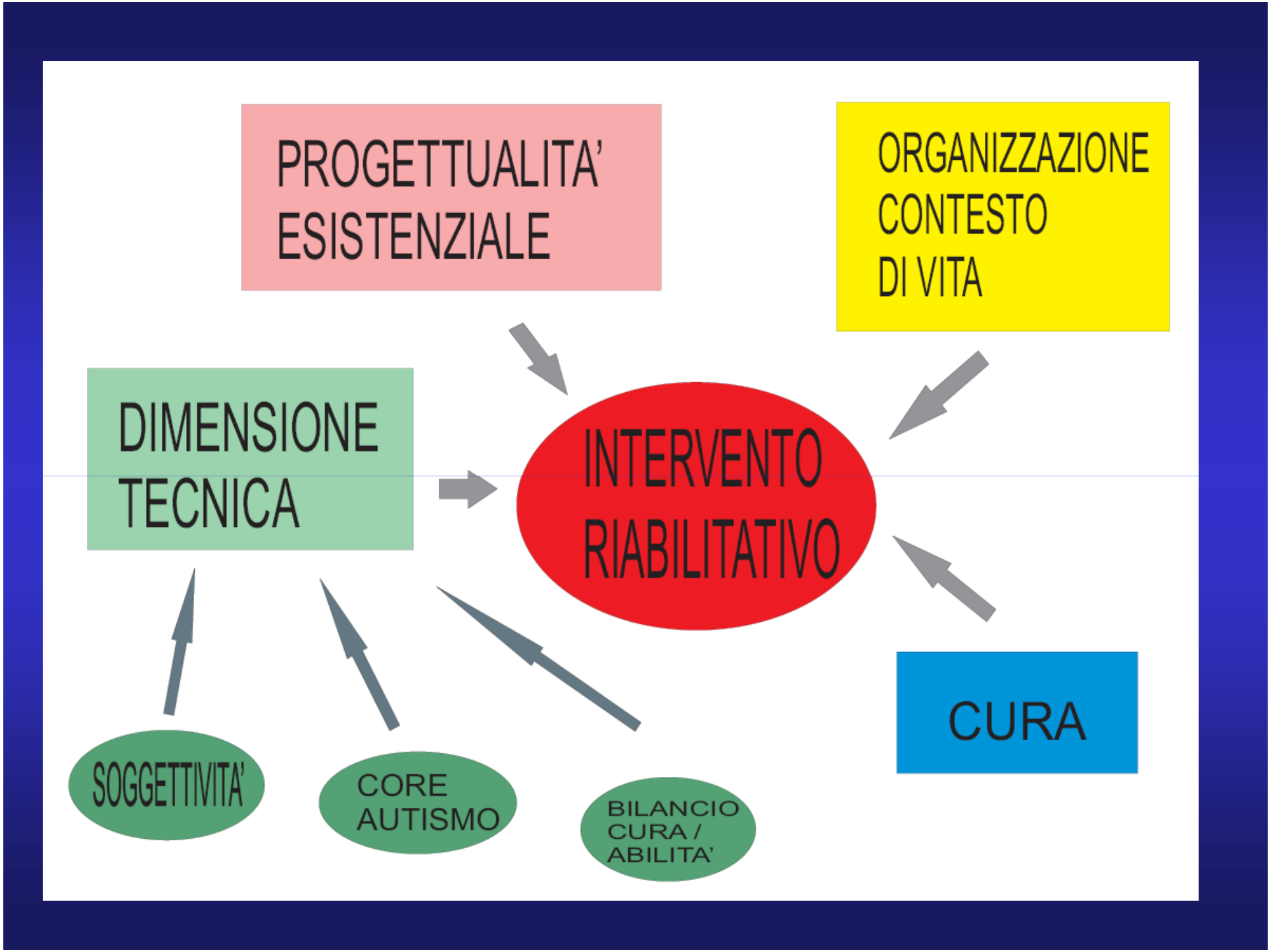
- Connessione costante tra dimensione tecnica, progettualità esistenziale, cura e organizzazione del contesto di vita.
- Non solo la comprensione della fenomenologia dell'autismo, ma gli interventi stessi sono efficaci se "ecologici".
- Solo questa forte "coerenza" garantisce significatività.

Barale & Ucelli, 2006
Barale et al, NOOS, 2009

La dimensione tecnica:

- caratteristiche nucleari dell'autismo
- bilancio e alla "cura delle abilità" presenti, assenti o emergenti
- dimensione personologica: "SOGGETTIVITA'"

Rischio di trascurare la soggettività!


PROGETTUALITA' ESISTENZIALE
ORGANIZZAZIONE CONTESTO DI VITA
DIMENSIONE TECNICA
INTERVENTO RIABILITATIVO
CURA
SOGGETTIVITA'
CORE AUTISMO
BILANCIO CURA / ABILITA'

- Intervento ecologico
- Soggettività
- From shared action to shared mind → Problem solving condiviso
- Imitazione

La soggettività

- Implementare comunicazione, espressione e capacità di scelta
- per proporre attività che tengano conto dell'inclinazione individuale (motivazione)

Quali interventi riabilitativi per l'autismo (1)

Non esiste un'unica risposta → l'intervento va il più possibile PERSONALIZZATO

- Per la persona high functioning: lavoro di interfaccia su contesto e persona autistica → reale inclusione sociale
- Per le persone autistiche con ritardo: creazione di contesti di vita e integrazione adatti

Quali interventi riabilitativi per l'autismo (2)

- Ma sappiamo intanto come **non** devono essere i contesti di abilitazione e vita per persone autistiche:
- ad esempio è un grave errore (dovrebbe essere considerata una *malpractice*) mescolare persone autistiche e persone con disturbi psicotici

Quali interventi riabilitativi per l'autismo (3)

Principi generali:

- Costanza
- Stabilità
- Strutturazione
- Continua organizzazione e riorganizzazione
- Attenzione per le caratteristiche dell'autismo
- Educazione strutturata permanente

Quali interventi riabilitativi per l'autismo (4)

- Aspetto naturalistico ed ecologico dell'intervento:stretta connessione tra attività abilitative e progettualità complessiva di vita
- Lavoro "vero" / significativo
- Il "fare insieme" (il problem solving condiviso:"from shared actions to shared minds")
- Monitoraggio dei CP; centratura sulle soggettività / comunicazione-motivazione

Le persone con autismo hanno molte difficoltà ad iniziare loro stesse l'interazione e a mantenere un qualche coinvolgimento se collocati in contesti non strutturati (Sigman, 1997)

- Intervento ecologico
- Soggettività
- From shared actions to shared minds → Problem solving condiviso
- Imitazione

“From shared actions to shared minds”

- Contesti adatti, strutturati
- Gli operatori attivamente iniziano l’interazione e mantengono la prossimità con la persona con autismo
- Le persone autistiche rispondono alle proposte di coinvolgimento sociale molto di più di quanto si pensi
- Le due figure “fanno insieme”

"From shared actions to shared minds": il ruolo del contesto

- Difficoltà delle persone autistiche ad intendere le intenzioni dell'interlocutore umano se essa è mediata solo dalla componente motoria
- Prendere alla lettera o in modo rigidamente semantico il significato delle cose…

“From shared actions to shared minds”: il ruolo del contesto

…ma se l’attribuzione di senso e di intenzioni è mediata da un ricco contesto semantico-pragmatico condiviso allora riescono ad identificare l’intenzione….e non hanno difficoltà a comprendere “cosa” e “perché”.

(Barale & Ucelli, 2006)

…ancora sul "problem solving condiviso"

Questo è il fondamento del "problem solving condiviso": dove si vede che disprassia, deficit di EF e sentimento di insufficienza del "sé-agente" nell'autismo non sono dei dati solo statici, immutabili, puramente "difettuali".

- Intervento ecologico
- Soggettività
- From shared actions to shared minds → Problem solving condiviso
- Imitazione

Clinical Neuropsychiatry (2007) 4, 5-6, 208-222

AUTISM – MORE THAN THE MIRROR SYSTEM[1]

Michael A. Arbib

Abstract

A number of studies have suggested an important role for defects in mirror neurons in developmental problems that lead to autism. My aim is to place this in perspective by

- stressing the importance of mirror neuron systems (note plural), while
- denying that mirror neurons do "it" (imitation, language, prevent autism) all by themselves

We must go both "within the mirror" to study the working of mirror systems in more detail and "beyond the mirror" to study mirror neuron systems within the context of larger neural systems for imitation, empathy and language. The present paper approaches this as follows: First, I summarize some basic characteristics of autism spectrum disorder (ASD) and mirror neuron systems (MNSs) and then present an influential view linking MNS and ASD (Williams et al. 2001). MNS activity characterizing goals and actions must be bound to other neural systems recognizing agents and objects – a point that is emphasized in a brief detour into the problem of alien voices and hands in schizophrenia (Arbib & Mundhenk 2005) – and I will argue that defects in binding of mirror neuron activity may be an important contributor to some deficits in ASD. I then use an fMRI study of imitation of facial expressions of emotion (Dapretto et al. 2006) to show that children with ASD can develop compensatory strategies by exploiting different neural mechanisms to capture some aspects of a socially relevant behavior. I complement discussion of the relevance of mirror neurons to the analysis of ASD by also considering approaches based on Theory of Mind and briefly discuss the roles of the amygdala and other brain regions. Finally, I suggest the promise of incremental computer modeling of "the Mirror System and Beyond."

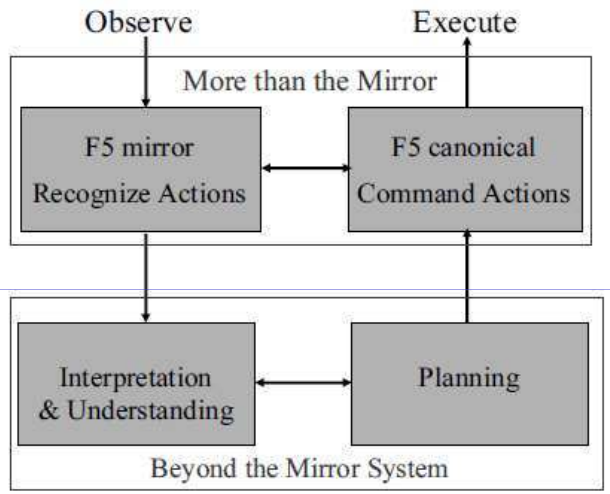


Figure 1. *Understanding and planning involve far more than the mirror systems*

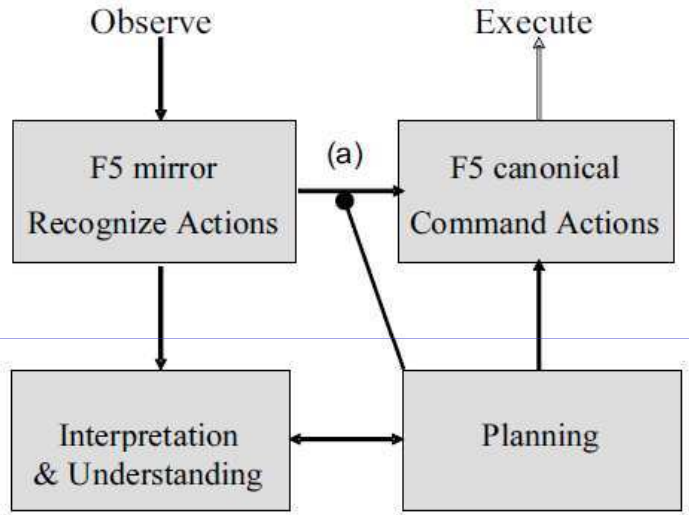
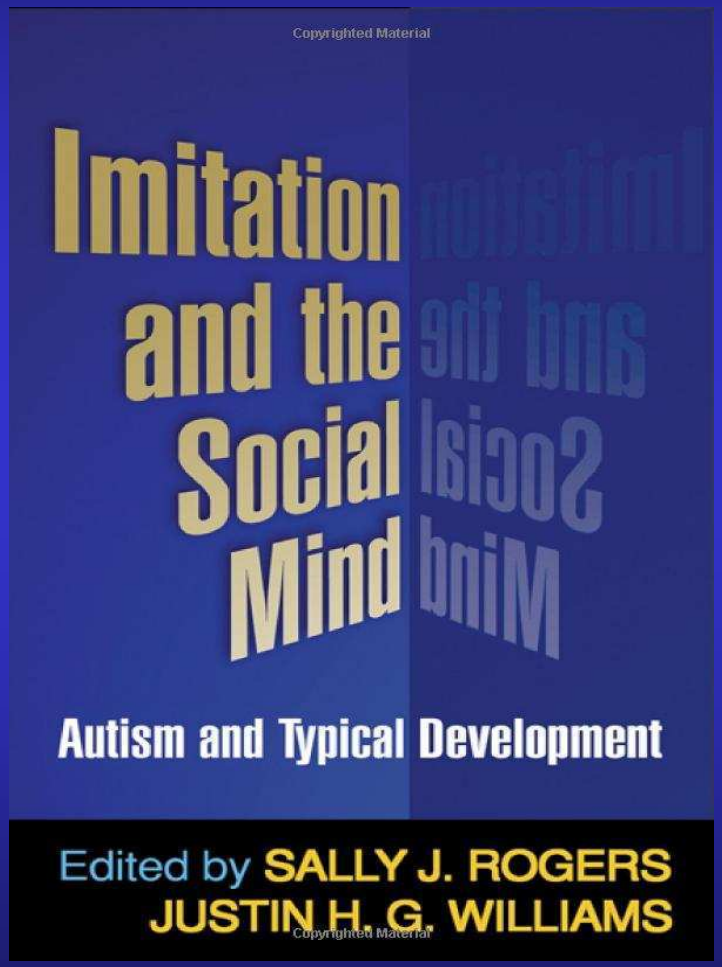


Figure 2. *Inhibiting a direct path from action observation to action execution to block echopraxia*

Clinical Neuropsychiatry (2007) 4, 5-6, 208-222



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Opinion

Cell PRESS

Unbroken mirrors: challenging a theory of Autism

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The 'broken mirror' theory of autism has received considerable attention far beyond the scientific community. This theory proposes that the varied social–cognitive difficulties characteristic of autism could be explained by dysfunction of the mirror neuron system, thought to play a role in imitation. We examine this theory and argue that explaining typical imitation behavior, and the failure to imitate in autism, requires much more than the mirror neuron system. Furthermore, evidence for the role of the mirror neuron system in autism is weak. We suggest the broken mirror theory of autism is premature and that better cognitive models of social behavior within and beyond the mirror neuron system are required to understand the causes of poor social interaction in autism.

thus, implies a three-way relationship between a brain system (the MNS), a behavior (imitation) and a disorder (autism) (Figure 2). Some versions of the broken mirror theory take a broader scope than imitation [7] and, drawing on speculations about MNS contributions to empathy [11], theory of mind [3] and language [4], propose that damage to the MNS could cause problems in all these areas [7]. However, in this opinion paper we focus primarily on the evidence for imitation as a key link between the MNS and autism because it is the only social–cognitive ability for which there is both evidence of MNS involvement [2] and some documented deficits in autism [10]

We will first examine the theory and evidence linking mirroring regions of the brain to imitation (Figure 2, arrow a), and imitation to autism (Figure 2, arrow b). We then

- People with autism show an enhanced automatic imitation effect (Bird et al, Proc. Biol. Sci. 2007; Treffert, 2009; Ey, 1950)
- The fact that children with autism can imitate but tend not to do so without instruction suggests that their difficulties might arise from problems with knowing when and what to imitate
- A reduced sensitivity to social cuesis well-documented in autism and could lead to atypical imitation behavior
- Children with autism can perform a variety of imitation tasks correctly when they are explicitly instructed to imitate (Hamilton et al, Neuropsychologia, 2007)

Unbroken mirrors in autism

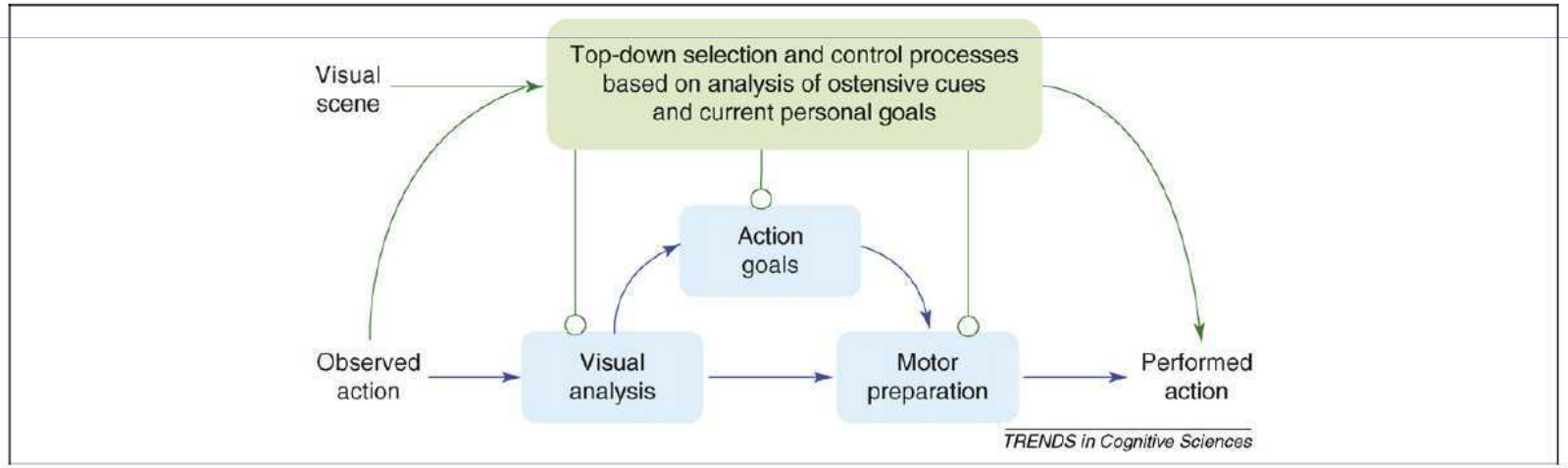
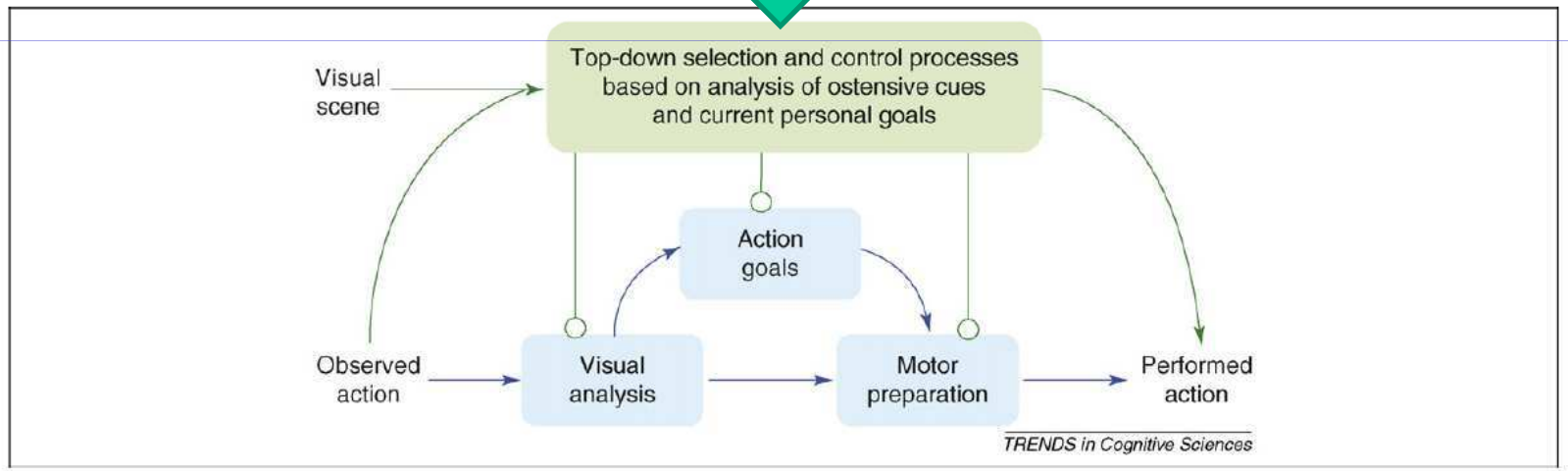


Figure 3. A possible cognitive model of imitation behavior. This figure illustrates some of the cognitive components that might underlie imitation behavior. Previous work [16,26] suggests that successful imitation involves at least three distinct types of representation: visual analysis of the observed action, extraction of a more abstract goal or semantic content and a motor plan for performing the action (blue boxes and lines). These all could be embedded in the core MNS. However, there is increasing evidence that imitation is subject to selection and top-down control processes, for example, based on the ostensive cues given by the observed actor (green boxes and lines) or based on the individual's current motivation. This selection could act at any stage of the imitation process to reduce or enhance imitation behavior. Thus, normal imitation depends on normal processing of communicative and ostensive cues and normal top-down selection and control systems. One or both of these processes might be abnormal in autism [20,26].

SOCIAL AND COMMUNICATION IMPAIRMENT IN AUTISM (CORE)



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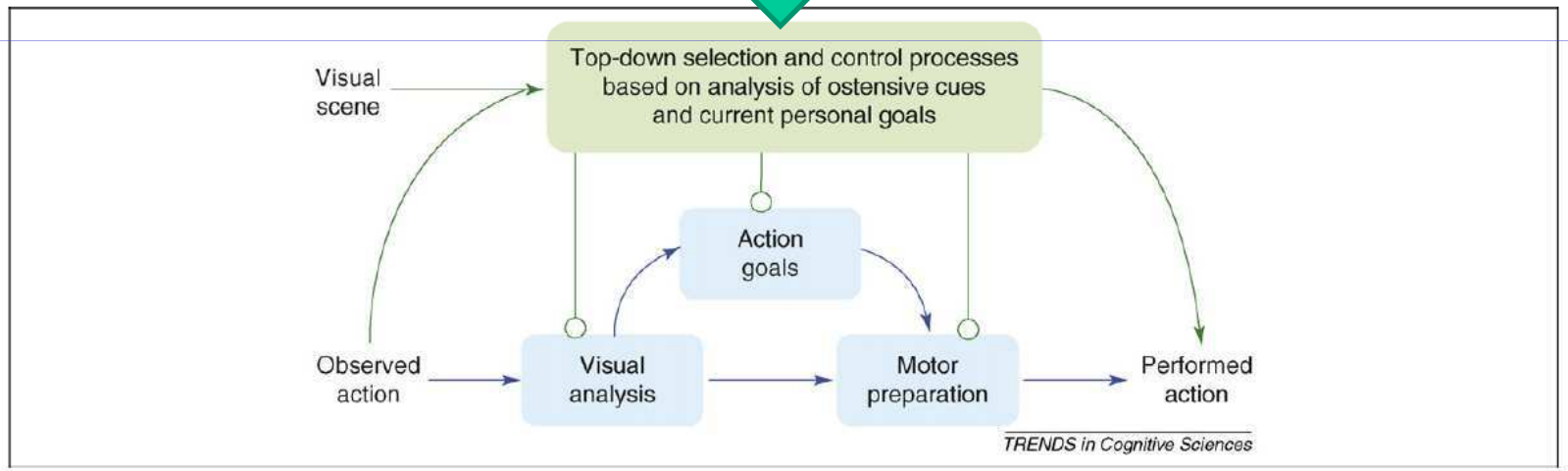
REHABILITATION MODEL "SHARED PROBLEM SOLVING"

SOCIAL AND COMMUNICATION IMPAIRMENT IN AUTISM (CORE)



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IL TRATTAMENTO FARMACOLOGICO

- Pochi RCT, mancano studi di effectiveness, basso numero di pazienti
- In uso nel mantenimento oppure nella sedazione di stati acuti
- **COMUNQUE non devono mai sostituirsi ad un adeguato intervento riabilitativo**
  (Malone & Waheed, 2009)

REVIEW ARTICLE

Drugs 2009; 69 (5): 535-548
0012-6667/09/0005-0535/$55.55/0

The Role of Antipsychotics in the Management of Behavioural Symptoms in Children and Adolescents with Autism

Richard P. Malone and *Ayesha Waheed*

Drexel University College of Medicine, Friends Hospital, Philadelphia, Pennsylvania, USA

Antipsychotics are beneficial for reducing problematic behaviours and improving overall functioning in patients with autism. These drugs should always be used as an adjunctive treatment to other interventions such as psychosocial and educational programmes. Among anti-

ATTENZIONE AI QUADRI COMPORTAMENTALI DA CAUSE MEDICHE E NEUROLOGICHE

USO INAPPROPRIATO AP!

Risk Factors of Acute Behavioral Regression in Psychiatrically Hospitalized Adolescents with Autism

Didier Périsse[1]; Claire Amiet[1,3]; Angèle Consoli[1,3]; Marie-Vincente Thorel[1]; Isabelle Gourfinkel-An[2]; Nicolas Bodeau[1]; Vincent Guinchat[1]; Catherine Barthélémy[4]; David Cohen[1,3]

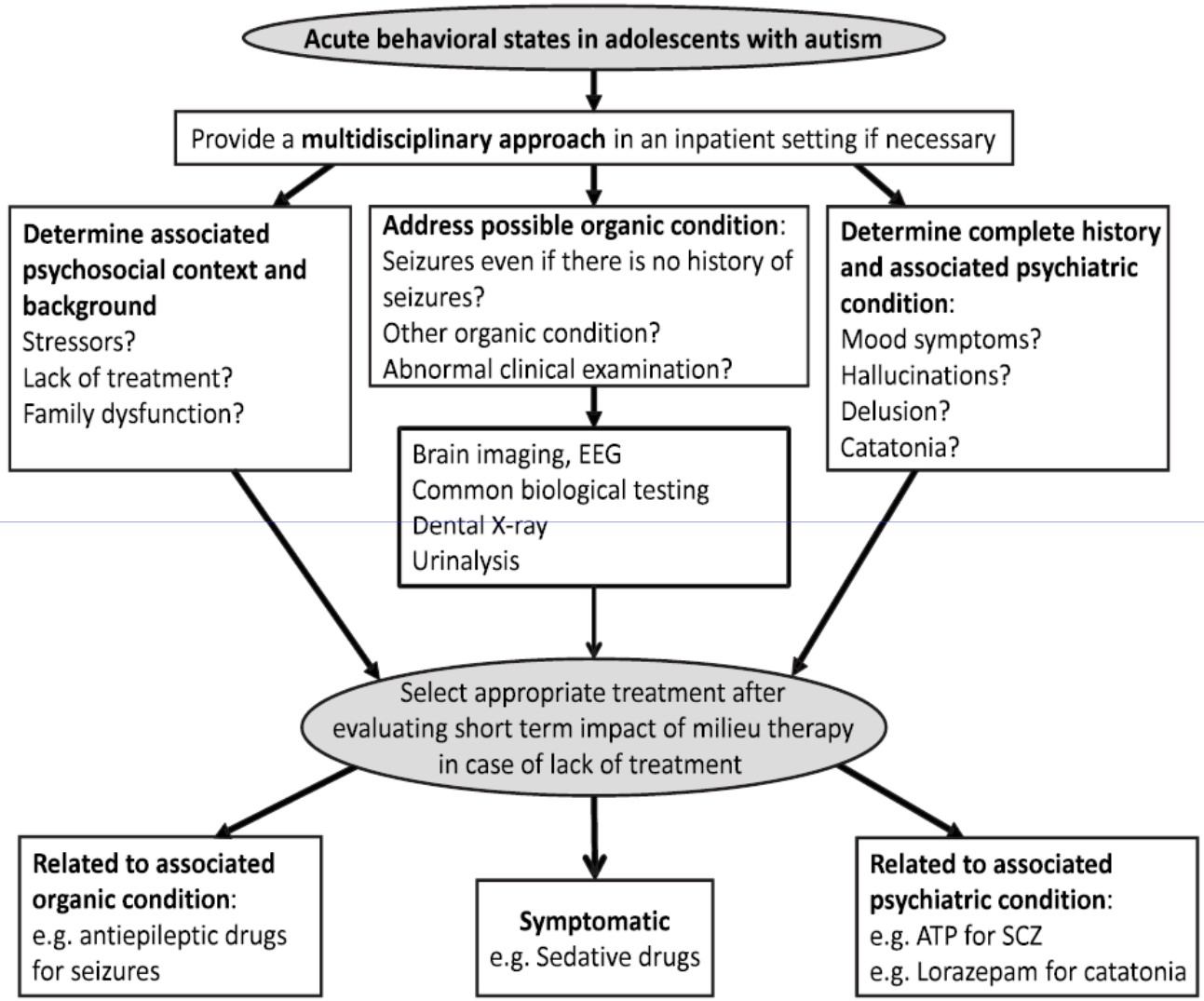
Abstract

Aim: During adolescence, some individuals with autism engage in severe disruptive behaviors, such as violence, agitation, tantrums, or self-injurious behaviors. We aimed to assess risk factors associated with very acute states and regression in adolescents with autism in an inpatient population. **Method:** Between 2001 and 2005, we reviewed the charts of all adolescents with autism (N=29, mean age=14.8 years, 79% male) hospitalized for severe disruptive behaviors in a psychiatric intensive care unit. We systematically collected data describing socio-demographic characteristics, clinical variables (severity, presence of language, cognitive level), associated organic conditions, etiologic diagnosis of the episode, and treatments. **Results:** All patients exhibited severe autistic symptoms and intellectual disability, and two-thirds had no functional verbal language. Fifteen subjects exhibited epilepsy, including three cases in which epilepsy was unknown before the acute episode. For six (21%) of the subjects, uncontrolled seizures were considered the main cause of the disruptive behaviors. Other suspected risk factors associated with disruptive behavior disorders included adjustment disorder (N=7), lack of adequate therapeutic or educational management (N=6), depression (N=2), catatonia (N=2), and painful comorbid organic conditions (N=3). **Conclusion:** Disruptive behaviors among adolescents with autism may stem from diverse risk factors, including environmental problems, comorbid acute psychiatric conditions, or somatic diseases such as epilepsy. The management of these behavioral changes requires a multidisciplinary functional approach.

Key words: autism, adolescence, acute behavioral state, regression, intellectual disability

J Can Acad Child Adolesc Psychiatry 19:2 May 2010

Figure 2. Acute behavioral states in adolescents with autism: a multimodal framework for evaluation and treatment.



EEG = electroencephalography; ATP = antipsychotic drug; SCZ = schizophrenia

Research in Developmental Disabilities 31 (2010) 743–749

Contents lists available at ScienceDirect

Research in Developmental Disabilities

Psychopathology: Differences among adults with intellectually disabled, comorbid autism spectrum disorders and epilepsy

Kimberly R.M. Smith *, Johnny L. Matson

Department of Psychology, Louisiana State University, United States

differences were found on the self-injury subscale and disruptive behavior subscale. Trend analysis demonstrated that individuals with ID expressing combined co-morbid ASD and epilepsy were significantly more impaired than the control group (ID only) or groups containing only a single co-morbid factor with ID (ASD or epilepsy only) on these four subscales. Implications of these findings in the context of known issues in ID, epilepsy, and ASD, current assessment practices among these populations and associated challenges are discussed.

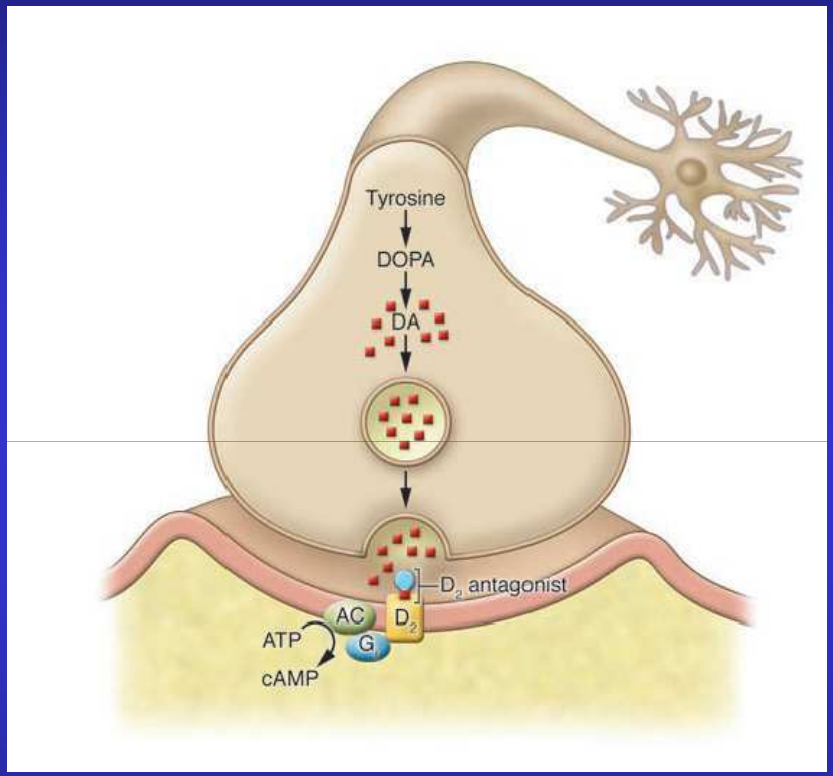
Antipsychotics in the treatment of autism

David J. Posey, Kimberly A. Stigler, Craig A. Erickson, and Christopher J. McDougle

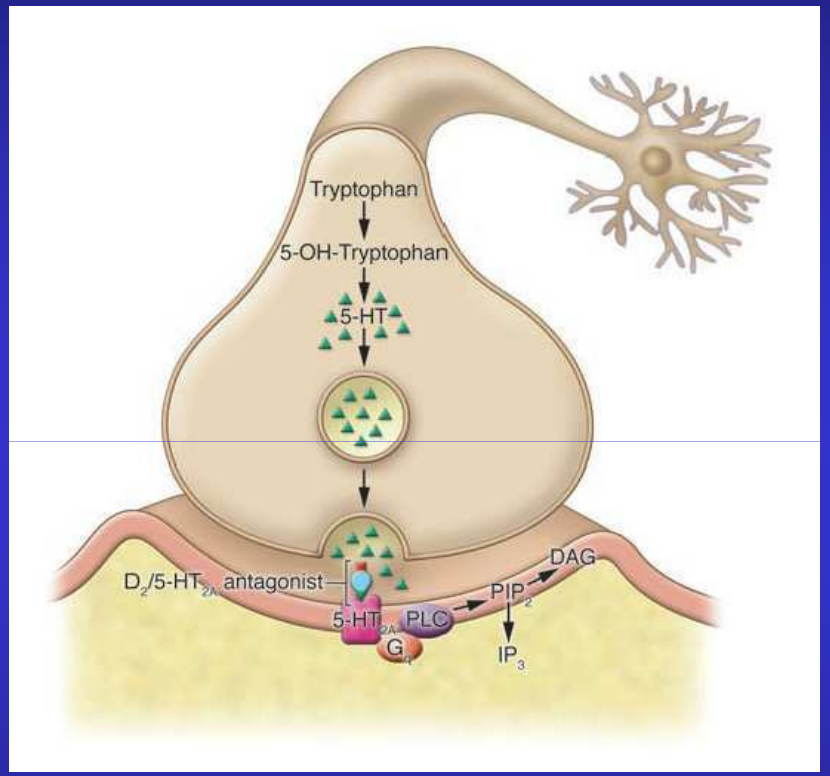
Christian Sarkine Autism Treatment Center, Department of Psychiatry, Indiana University School of Medicine, Indianapolis, Indiana, USA.

Atypical antipsychotics commonly used to treat severe behavioral symptoms in PDDs

Drug	Study (ref.)	Symptoms improved	Notable side effects
Risperidone			
	2.9 mg/d > placebo in 31 adults with PDD (13)	Aggression, irritability, repetitive behavior	Sedation, weight gain
	1.8 mg/d > placebo in 101 children with autism (15)	Aggression, hyperactivity, irritability, repetitive behavior	Hypersalivation, sedation, weight gain
	1.2 mg/d > placebo in 79 children with PDD (16)	Aggression, hyperactivity, irritability, repetitive language and behavior, social withdrawal	Sedation, weight gain
	1 mg/d > placebo in 40 young children with PDD (69)	Aggression, hyperactivity, nonverbal communication, social responsiveness	Sedation, weight gain
	1.1 mg/d > placebo in 24 preschool children with PDD (70)	Mild improvement in autism severity	Hypersalivation, weight gain
Olanzapine	10 mg/d > placebo in 11 children with autism (74)	Global improvement	Sedation, weight gain
Quetiapine	No placebo-controlled studies; 4 open-label investigations have reported 22%–60% response rate (refs. 75–78; N = 6, 9, 20, and 10, respectively)	Aggression, hyperactivity, inattention	Agitation, sedation, weight gain
Ziprasidone	No placebo-controlled studies; 2 open-label investigations have reported 50%–70% response rate (refs. 80, 81; N = 12 and 10, respectively)	Aggression, irritability	Sedation, weight gain (mild)
Aripiprazole	No placebo-controlled studies; 2 open-label investigations have reported 92%–100% response rate (refs. 84, 85; N = 5 and 13, respectively)	Aggression, irritability	Weight gain (mild)



Simplified schematic of a DA synapse showing synthesis of DA, a postsynaptic D_2 receptor, and intracellular mechanisms. Most conventional and atypical antipsychotics block DA D_2 receptors. The D_2 receptor is coupled by an inhibitory G protein (G_i) to adenylyl cyclase (AC), which converts ATP to cAMP, a secondary messenger.



Simplified schematic of a serotonin (5-HT) synapse showing synthesis of 5-HT, a postsynaptic 5-HT_2 receptor, and intracellular mechanisms. In contrast to conventional antipsychotics, most atypical antipsychotics block 5-HT_2 receptors. The 5-HT_2 receptor is coupled by a G protein (G_q) to phospholipase C (PLC). Phospholipase C hydrolyzes membrane-bound phosphatidyl inositol (PIP_2), generating 2 secondary messengers, inositol triphosphate (IP_3) and diacylglycerol (DAG).

Selective serotonin reuptake inhibitors (SSRIs) for autism spectrum disorders (ASD) (Review)

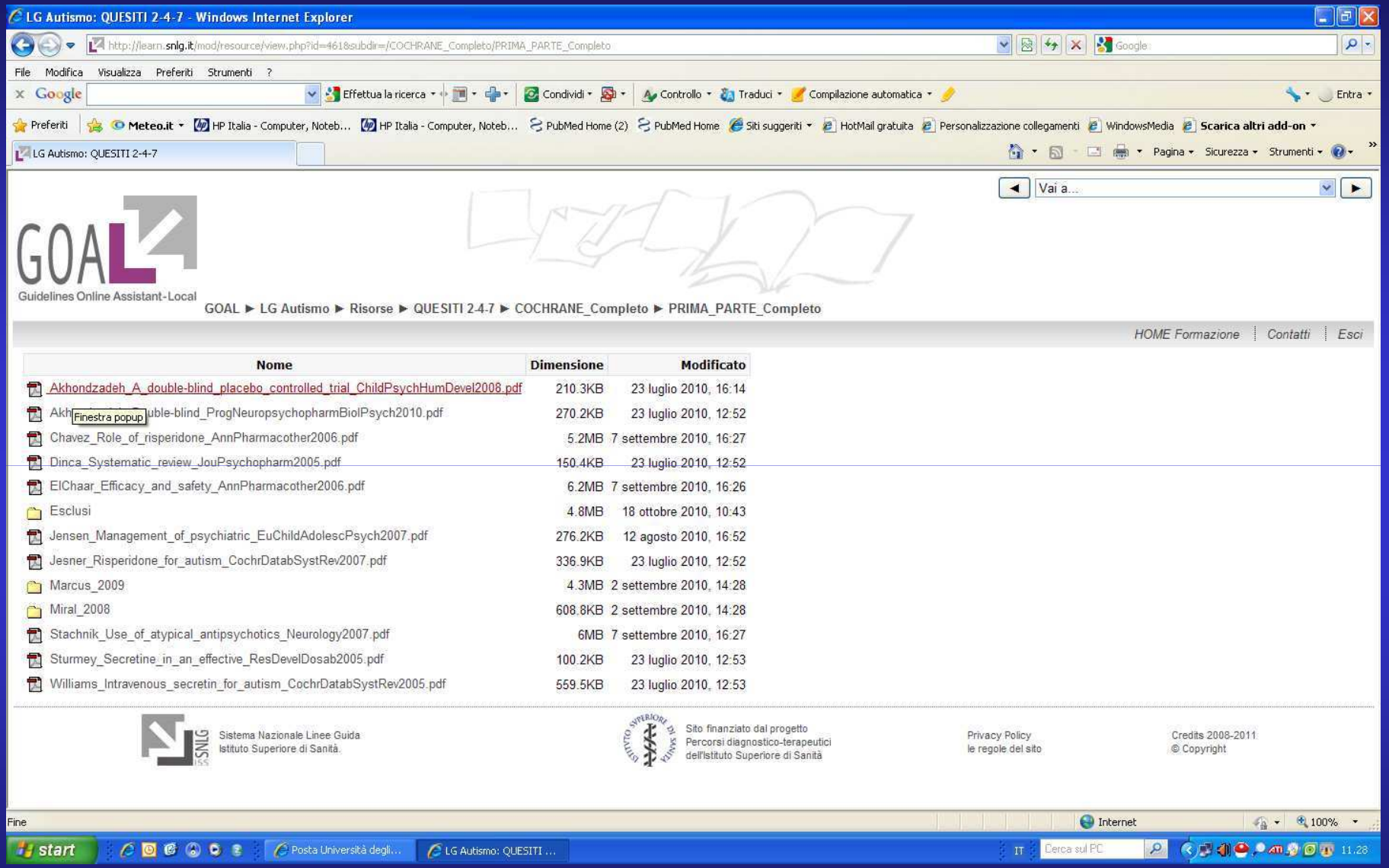
Williams K, Wheeler DM, Silove N, Hazell P

Main results

Seven RCTs with a total of 271 participants were included. Four SSRIs were evaluated: fluoxetine (two studies), fluvoxamine (two studies), fenfluramine (two studies) and citalopram (one study). Five studies included only children and two studies included only adults. Varying inclusion criteria were used with regard to diagnostic criteria and intelligence of participants. Seventeen different outcome measures were reported. Although more than one study reported data for Clinical Global Impression (CGI) and obsessive-compulsive behaviour (OCB), different tool types or components of these outcomes were used in each study. As such, data were unsuitable for meta-analysis. One large, high quality study in children showed no evidence of positive effect of citalopram. Two small studies in adults showed positive outcomes for CGI and OCB; one study showed improvements in aggression, and another in anxiety.

Authors' conclusions

There is no evidence of effect of SSRIs in children and emerging evidence of harm. There is limited evidence of the effectiveness of SSRIs in adults from small studies in which risk of bias is unclear.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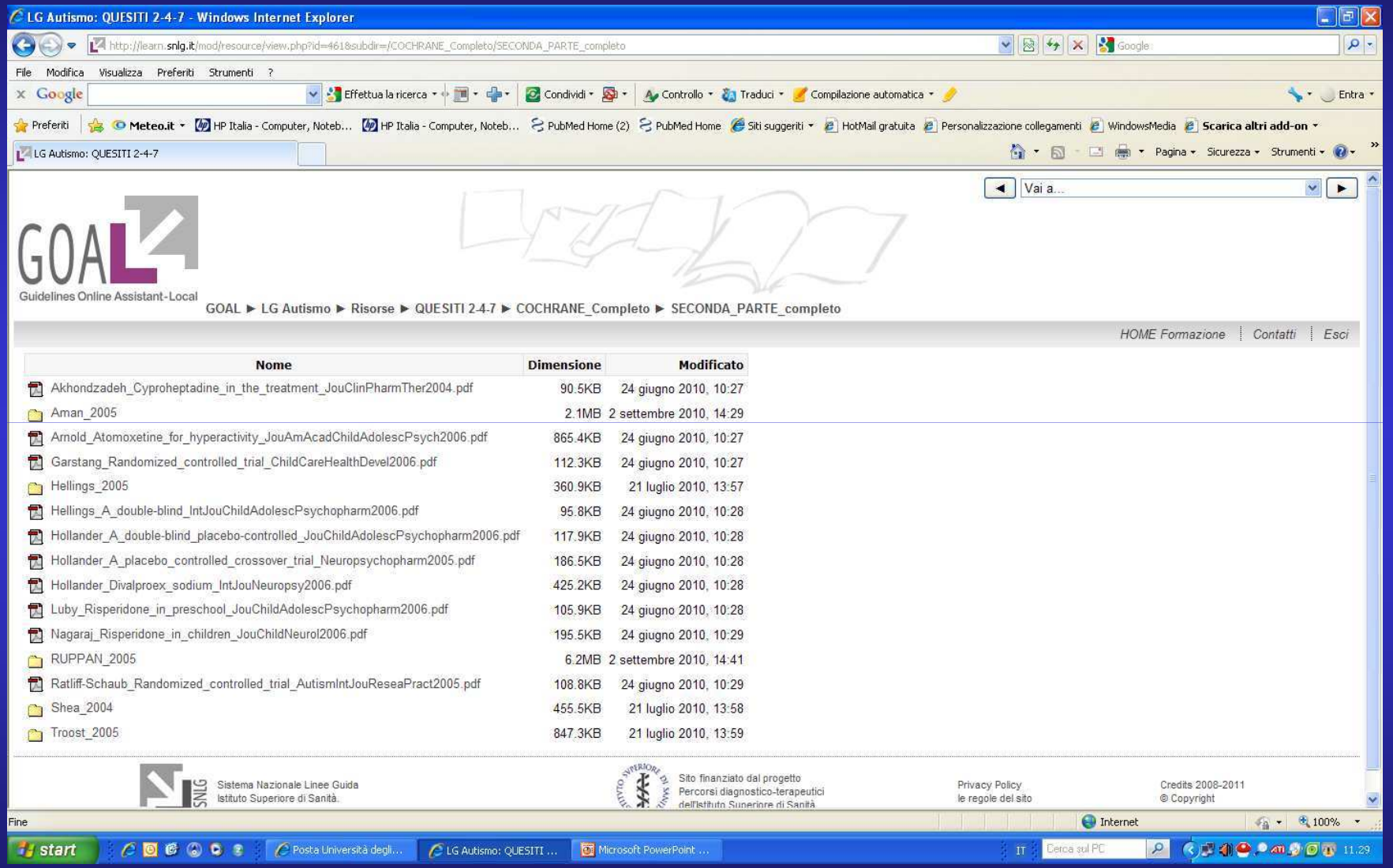
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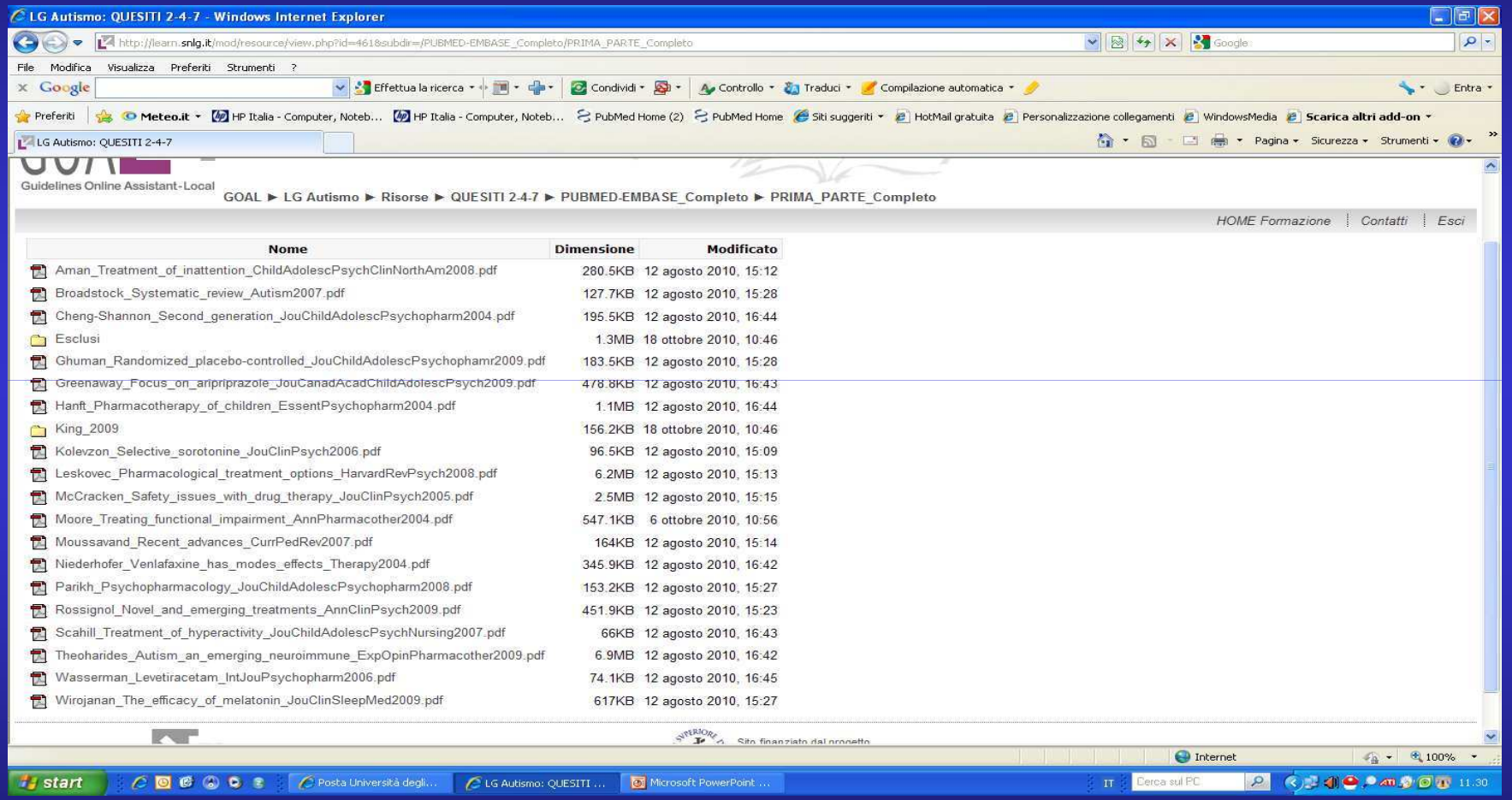
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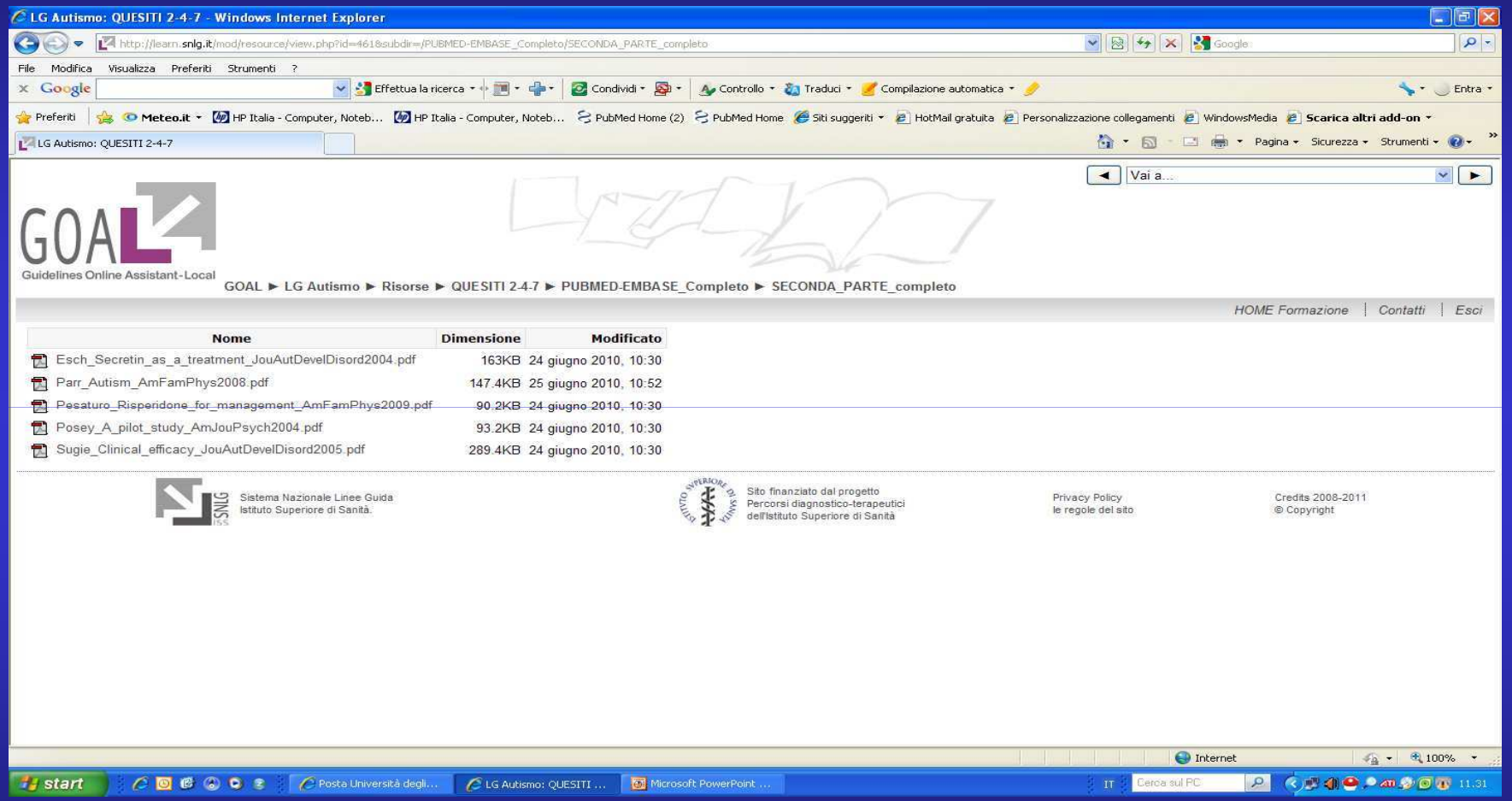
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Elementi fondamentali

1. I CP hanno in genere uno scopo per la persona che li manifesta

2. L'assessment funzionale serve per identificare tale scopo (o tali scopi)

3. Lo scopo dell'intervento è l'educazione e lo sviluppo di comportamenti alternativi, non la semplice riduzione del CP. L'intervento cioè deve essere costitutivo di abilità.

Elementi fondamentali

4. Il CP ha spesso più scopi e richiede molteplici interventi.

5. L'intervento richiede il cambiamento non solo degli individui ma del Sistema di relazione e del contesto.

6. La meta finale di ogni intervento è rivolta non al singolo problema ma alla persona, al suo stile di vita.

Conclusioni

"The disorders in language and social interaction observed in autism (with the rigid insistence on sameness, the isolation, and the communication impairment) would be the negative consequences of this (circuits alteration) at the higher behavioral level"

"However, these same alterations, as well as causing deficits and disability, could promote the generation of an intense world of emotions, interests, abilities and capacities, which are often unexpected and sometimes exceptional"

Boso et al, Funct Neurol 2010

The Intense World Syndrome – an alternative hypothesis for autism

Henry Markram, Tania Rinaldi and Kamila Markram*

Brain Mind Institute, Ecole Polytechnique Fédérale de Lausanne, Switzerland

Review Editors: Joseph LeDoux, Center for Neural Science, New York University, USA
Jacqueline N. Crawley, Laboratory of Behavioral Neuroscience, National Institute of Mental Health, USA

Autism is a devastating neurodevelopmental disorder with a polygenetic predisposition that seems to be triggered by multiple environmental factors during embryonic and/or early postnatal life. While significant advances have been made in identifying the neuronal structures and cells affected, a unifying theory that could explain the manifold autistic symptoms has still not emerged. Based on recent synaptic, cellular, molecular, microcircuit, and behavioral results obtained with the valproic acid (VPA) rat model of autism, we propose here a unifying hypothesis where the core pathology of the autistic brain is hyper-reactivity and hyper-plasticity of local neuronal circuits. Such excessive neuronal processing in circumscribed circuits is suggested to lead to hyper-perception, hyper-attention, and hyper-memory, which may lie at the heart of most autistic symptoms. In this view, the autistic spectrum are disorders of hyper-functionality, which turns debilitating, as opposed to disorders of hypo-functionality, as is often assumed. We discuss how excessive neuronal processing may render the world painfully intense when the neocortex is affected and even aversive when the amygdala is affected, leading to social and environmental withdrawal. Excessive neuronal learning is also hypothesized to rapidly lock down the individual into a small repertoire of secure behavioral routines that are obsessively repeated. We further discuss the key autistic neuropathologies and several of the main theories of autism and re-interpret them in the light of the hypothesized *Intense World Syndrome*.

Keywords: autism, microcircuit, connectivity, plasticity, neocortex, amygdala, valproic acid